CLAIMS

What is claimed is:

1. A method of determining an efficacious dose of a compound administered to a subject for the purpose of modulating angiogenesis, comprising the step of

(a) administering the compound to a patient;

(b) monitoring a marker related to angiogenesis;

(c) constructing a standard curve; and

(d) determining the efficacious dose based on the standard curve.

2. The method of claim 1, wherein said angiogenesis is modulated to treat or prevent conditions associated with angiogenesis including conditions manifested by cell proliferation, cell differentiation, or cell survival.

3. The method of claim 2, wherein said conditions associated with cell proliferation is selected from the group consisting of cancer, arthritis, endometriosis, and ocular neovascularization.

4. The method of claim 1, wherein said compound is selected from the group consisting of a receptor agonist and a receptor antagonist.

5. The method of claim 4, wherein said compound is a receptor antagonist that inhibits a receptor involved in angiogenesis.

6. The method of claim 5, wherein said receptor involved in angiogenesis is selected from the group consisting of Flt-1 and Flk-1.

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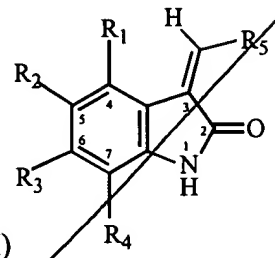
7. The method of claim 5, wherein said drug is an indolinone compound, having the structure set forth in formula I:



(I)

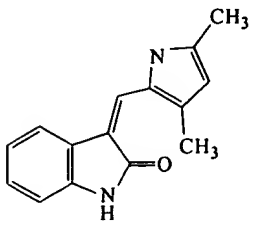
wherein

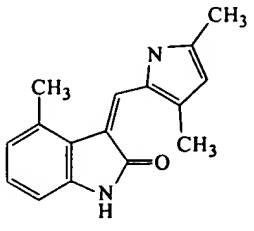
(a) R_1, R_2, R_3, and R_4 are selected from the group consisting of hydrogen, trihalomethyl, hydroxyl, amine, thioether, cyano, alkoxy, alkyl, amino, bromo, fluoro, chloro, iodo, mercapto, thio, cyanoamido, alkylthio, aryl, heteroaryl, carboxyl, ester, oxo, alkoxycarbonyl, alkenyl, alkoxy, nitro, alkoxyl, and amido moieties; and

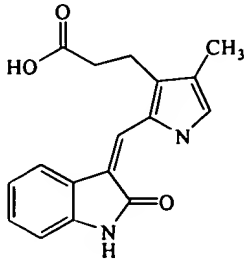
(b) R_5 is an optionally substituted aryl or heteroaryl cyclic moiety;

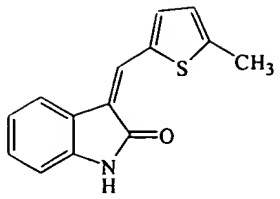
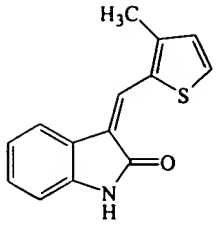
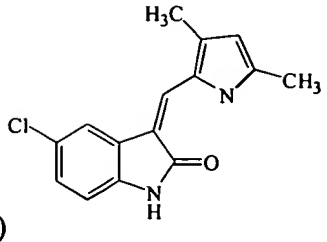
or a pharmaceutically acceptable salt, ester, amide, prodrug, isomer, and metabolite thereof.

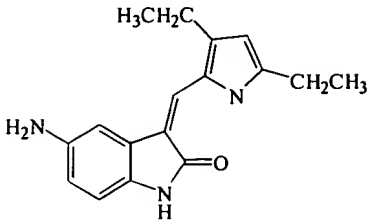
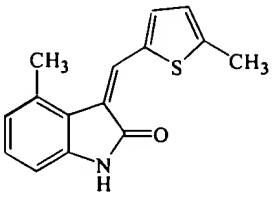
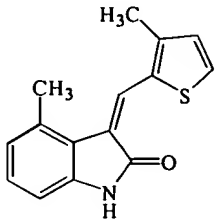
8. The method of claim 7, wherein said indolinone compound is selected from the group consisting of

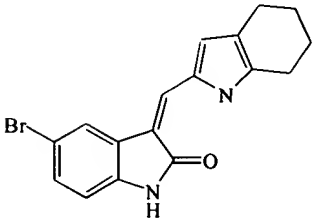
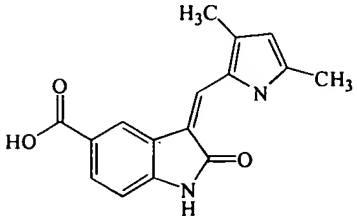
(a)  ,

(b)  ,

(c)  ,

(d)  , (e)  , (f)  ,

(g)  , (h)  , (i)  ,

(j)  , and (k)  .

9. The method of claim 1, wherein said marker is present in a sample obtained from said subject.

10. The method of claim 9, wherein said sample is selected from the group consisting of whole blood, a blood fraction, blood plasma, blood serum, cells isolated from blood, whole urine, a urine fraction, saliva, cells isolated from saliva, spinal fluid, amniotic fluids, and biopsy of endothelial cells.

11. The method of claim 10, wherein said sample comprises monocytes.

12. The method of claim 11 comprising the step of adding a receptor agonist to said sample.

13. The method of claim 12, wherein said receptor agonist enhances angiogenesis.

14. The method of claim 13, wherein said receptor agonist is vascular endothelial cell growth factor.

15. The method of claim 1, wherein said marker is selected from the group consisting of cell division, cell motility, cell proliferation, cell death, cell survival, cell differentiation, protein phosphorylation, protein expression, protein glycosylation, mRNA expression, cellular membrane potential, DNA division, DNA methylation, and post-translational modification of a protein.

16. The method of claim 1, wherein said marker is selected from the group consisting of DNA, RNA, mRNA, and protein.

17. The method of claim 1, wherein said step of monitoring a marker comprises the step of determining the presence or amount of said marker.

18. The method of claim 17, wherein said presence or amount of said marker is detected using an antibody.

19. The method of claim 17, wherein said presence or amount of said marker is determined by measuring blood clotting.

20. The method of claim 1, wherein said step of monitoring a marker related to angiogenesis comprises the step of determining the presence or amount of marker mRNA.

21. The method of claim 20, wherein said presence of marker mRNA is determined using reverse transcriptase polymerase chain reaction or a polynucleotide probe.

22. The method of any one of claims 1 and 15 - 21, wherein said marker is selected from the group consisting of tissue factor, CD40, u-PA, ETS-1, IL8, and t-PA.

23. The method of any one of claims 15 - 21, wherein said marker is present in a sample obtained from a subject.

24. The method of claim 1, wherein said step of monitoring a marker related to angiogenesis comprises the step of comparing said marker to a standard.

25. A method of treating a disease using the efficacious dose of a drug determined by the method of claim 1.

26. The method of claim 25, wherein said disease is related to angiogenesis.